Complete Summary

GUIDELINE TITLE

Drug-drug interactions between HAART, medications used in substance use treatment, and recreational drugs.

BIBLIOGRAPHIC SOURCE(S)

New York State Department of Health. Drug-drug interactions between HAART, medications used in substance use treatment, and recreational drugs. New York (NY): New York State Department of Health; 2005 Jul. 22 p. [57 references]

GUIDELINE STATUS

This is the current release of the guideline.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory information has been released:

- On January 19, 2005, the U.S. Food and Drug Administration (FDA) issued a public health advisory about recent safety-related changes to the nevirapine (Viramune®) label and about appropriate use of HIV triple combination therapy containing nevirapine. The Indications and Usage section now recommends against starting nevirapine treatment in women with CD4+cell counts greater than 250 cells/mm^3 unless benefits clearly outweigh risks. This recommendation is based on a higher observed risk of serious liver toxicity in patients with higher CD4 cell counts prior to initiation of therapy. See the FDA Web site for more information.
- On June 10, 2005, Bristol-Myers Squibb and FDA notified healthcare professionals of revisions to the WARNINGS, PRECAUTIONS/Pregnancy and Information for Patients, and PATIENT INFORMATION sections of the prescribing information for Sustiva (efavirenz), indicated in the treatment of HIV-1 infection. The revisions are a result of four retrospective reports of neural tube defects in infants born to women with first trimester exposure to Sustiva, including three cases of meningomyelocele and one Dandy Walker Syndrome. As Sustiva may cause fetal harm when administered during the first trimester to a pregnant woman, pregnancy should be avoided in women receiving Sustiva. An antiretroviral pregnancy registry has been established to monitor fetal outcomes of pregnant women exposed to Sustiva. See the FDA Web site for more information.

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SCOPE

DISEASE/CONDITION(S)

- Human immunodeficiency virus (HIV) infection
- Conditions associated with drug interactions encountered in HIV-infected patients using highly active antiretroviral therapy (HAART) as well as medications used in substance use treatment and recreational drugs

GUIDELINE CATEGORY

Management
Prevention
Risk Assessment

CLINICAL SPECIALTY

Allergy and Immunology
Family Practice
Infectious Diseases
Internal Medicine
Pharmacology

INTENDED USERS

Advanced Practice Nurses
Health Care Providers
Physician Assistants
Physicians
Public Health Departments
Substance Use Disorders Treatment Providers

GUIDELINE OBJECTIVE(S)

- To present an overview of known and potential interactions between medications used in the treatment of substance use, recreational drugs, and highly active antiretroviral therapy (HAART)
- To provide guidelines for management of drug-drug interactions between HAART and medications used in substance use treatment and recreational drugs

TARGET POPULATION

Human immunodeficiency virus (HIV)-infected patients

INTERVENTIONS AND PRACTICES CONSIDERED

1. Conducting a thorough medication history at each visit, including
    - Prescription medications
    - Over-the-counter medications
    - Recreational drugs
    - Herbal and alternative therapies
2. Classifying common inhibitors, inducers, and substrates of the cytochrome P-450 (CYP450) system to predict significant drug interaction
3. Discussing potential drug interactions with patients receiving methadone or using recreational drugs before initiating antiretroviral therapy (ARV)
4. Monitoring patients receiving concurrent methadone or using recreational drugs and highly active antiretroviral therapy (HAART) for drug-interaction symptoms, such as withdrawal symptom or excess sedation and zidovudine toxicity (in patients taking methadone), as well as for signs of hepatotoxicity (in patients taking recreational drugs)
5. Reporting all prescribed HAART-related drug changes for patients receiving methadone to the patient's methadone maintenance program, particularly if changes include initiating efavirenz or nevirapine
6. Avoiding certain drug combinations likely to produce adverse reactions (refer to the original guideline document for details)

MAJOR OUTCOMES CONSIDERED

Morbidity/adverse effects associated with drug-drug interactions

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The Human Immunodeficiency Virus (HIV) Guidelines Program works directly with committees composed of HIV Specialists to develop clinical practice guidelines. These specialists represent different disciplines associated with HIV care, including infectious diseases, family medicine, obstetrics and gynecology, among others. Generally, committees meet in person 3-4 times per year, and otherwise conduct business through monthly conference calls.

Committees meet to determine priorities of content, review literature, and weigh evidence for a given topic. These discussions are followed by careful deliberation to craft recommendations that can guide HIV primary care practitioners in the delivery of HIV care. Decision making occurs by consensus. When sufficient evidence is unavailable to support a specific recommendation that addresses an important component of HIV care, the group relies on their collective best practice experience to develop the final statement. The text is then drafted by one member, reviewed and modified by the committee, edited by medical writers, and then submitted for peer review.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

General Recommendation

The clinician should conduct a thorough medication history at each visit that includes prescription medications, including those prescribed by other providers, over-the-counter medications, recreational drugs, and herbal/alternative therapies.

Drug Interactions Related to the Metabolism of Highly Active Antiretroviral Therapy (HAART)

Table 1 in the original guideline document shows the potential interactions among antiretroviral (ARV) agents and the most common medications used to treat substance use disorders according to how they are metabolized.

Drug Interactions with Methadone

Clinicians should discuss potential drug interactions with patients receiving methadone before initiating ARV therapy.

Clinicians should report all prescribed HAART-related drug changes for patients receiving methadone to the patient's methadone maintenance program.

Clinicians should monitor human immunodeficiency virus (HIV)-infected substance users receiving concurrent methadone and ARV therapy for symptoms of withdrawal and/or excess sedation when ARV therapy is initiated or changed.

Key Point:

Interactions between HAART and methadone may precipitate symptoms of oversedation or withdrawal.

Nucleoside/Nucleotide Reverse Transcriptase Inhibitors (NRTIs)

When using didanosine in patients receiving methadone, clinicians should consider using the enteric-coated capsule formulation because it does not lead to a clinically significant interaction when given concurrently with methadone.

Clinicians should monitor patients for symptoms of zidovudine toxicity, such as anemia, nausea, and headaches, when zidovudine and methadone are used concurrently.

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

Clinicians initiating a HAART regimen consisting of efavirenz or nevirapine in patients receiving methadone should contact the methadone maintenance program clinicians to ensure that the onset of withdrawal symptoms, if they occur, is promptly addressed by increasing the patient's methadone dose.

Clinicians prescribing methadone maintenance therapy should closely monitor patients when adding efavirenz or nevirapine to their ARV regimens.

Recreational Drugs and HAART

Clinicians should assess adherence and be alert for signs of hepatotoxicity in HIV-infected patients receiving HAART who are concurrently using recreational drugs.

See Appendix C in the original guideline document for a list of known drug interactions with HAART and recreational drugs.

Amphetamines

Clinicians should not prescribe ritonavir, even in low doses for boosting, if patients report using amphetamines.

Barbiturates

Clinicians should avoid co-administration of NNRTIs and phenobarbital.

Benzodiazepines

Clinicians should avoid concurrent use of alprazolam, midazolam, and triazolam with all protease inhibitors (PIs), delavirdine, and efavirenz.

Ecstasy (Methylenedioxy-methamphetamine [MDMA])

Clinicians should not prescribe protease inhibitors (PIs), even in low doses for boosting, if patients report using ecstasy or gamma hydroxybutyrate (GHB).

Psychotropics

Clinicians should consider medication interactions as a potential cause of mental status changes in persons receiving psychotropic medications and HAART.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is not specifically stated for each recommendation.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Improved understanding and appropriate management of known and potential interactions between medications used in the treatment of substance use, recreational drugs, and highly active antiretroviral therapy (HAART)

POTENTIAL HARMS

Refer to appendix D in the original guideline document for agents to be used with caution.

CONTRAINDICATIONS

CONTRAINDICATIONS

Refer to appendix D in the original guideline document for contraindicated combinations.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Following the development and dissemination of guidelines, the next crucial steps are adoption and implementation. Once practitioners become familiar with the content of guidelines, they can then consider how to change the ways in which they take care of their patients. This may involve changing systems that are part of the office or clinic in which they practice. Changes may be implemented rapidly, especially when clear outcomes have been demonstrated to result from the new practice such as prescribing new medication regimens. In other cases, such as diagnostic screening or oral health delivery, however, barriers emerge which prevent effective implementation. Strategies to promote implementation, such as through quality of care monitoring or dissemination of best practices, are listed and illustrated in the companion document to the original guideline (HIV clinical practice guidelines, New York State Department of Health; 2003), which portrays New York's HIV Guidelines Program. The general implementation strategy is outlined below.

- Statement of purpose and goal to encourage adoption and implementation of guidelines into clinical practice by target audience
- Define target audience (providers, consumers, support service providers)
    - Are there groups within this audience that need to be identified and approached with different strategies (e.g., HIV Specialists, family practitioners, minority providers, professional groups, rural-based providers)?
- Define implementation methods
    - What are the best methods to reach these specific groups (e.g., performance measurement consumer materials, media, conferences)?
- Determine appropriate implementation processes
    - What steps need to be taken to make these activities happen?
    - What necessary processes are internal to the organization (e.g., coordination with colleagues, monitoring of activities)?
    - What necessary processes are external to the organization (e.g., meetings with external groups, conferences)?
    - Are there opinion leaders that can be identified from the target audience that can champion the topic and influence opinion?
- Monitor progress
    - What is the flow of activities associated with the implementation process and which can be tracked to monitor the process?
- Evaluate
    - Did the processes and strategies work?
    - Were the guidelines implemented?
    - What could be improved in future endeavors?

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness
Safety

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

New York State Department of Health. Drug-drug interactions between HAART, medications used in substance use treatment, and recreational drugs. New York (NY): New York State Department of Health; 2005 Jul. 22 p. [57 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2005 Jul

GUIDELINE DEVELOPER(S)

New York State Department of Health - State/Local Government Agency [U.S.]

SOURCE(S) OF FUNDING

New York State Department of Health

GUIDELINE COMMITTEE

Substance Use Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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AIDS Institute: Diane Rudnick, Director, Substance Abuse Section, New York State Department of Health

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available from the New York State Department of Health AIDS Institute Web site.

Print copies: Available from Office of the Medical Director, AIDS Institute, New York State Department of Health, 5 Penn Plaza, New York, NY 10001; Telephone: (212) 268-6108

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- HIV clinical practice guidelines. New York (NY): New York State Department of Health; 2003. 36 p.

Electronic copies: Available from the New York State Department of Health AIDS Institute Web site.

Print copies: Available from Office of the Medical Director, AIDS Institute, New York State Department of Health, 5 Penn Plaza, New York, NY 10001; Telephone: (212) 268-6108

PATIENT RESOURCES

None available

NGC STATUS

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